Nanotechnology En Route from Bench to Bedside for Cancer Patients

NCI's 12 Platform Partnership Awards catalyze development of diagnostic, imaging, and therapeutic tools against multiple cancer types.

Among the issues that NCI grappled with in the design of its Cancer Nanotechnology Plan two years ago was the challenge of translation: how to ensure that discoveries would not rest inside a rarified academic world, but would move expeditiously towards clinical application to achieve genuine benefits for patients within three to five years. In other words, how we move great science from the bench to the bedside quickly.

Following months of planning and countless discussions with scientists and other members of the cancer community, the requisites emerged. Multidisciplinary teams. Academic institutions in collaboration with the private sector. Seamless networking. And product development plans.

On October 17, 2005, the NCI awarded 12 Cancer Nanotechnology Platform Partnership awards to recipients who had shaped their programs with those attributes front and center. The awards will total $35 million over five years, with $7 million awarded in the first year. The teams granted these awards are linked to NCI-designated Cancer Centers, and will create and implement new nanotechnology-based materials in six important areas spanning all key steps from prevention to detection to diagnosis to treatment to monitoring of efficacy.

Already, these teams are en route, taking their technological discoveries down carefully defined tracks to the clinic (see "*A Nano Cancer Gallery*" for more detail). According to NCI leadership, the projects cover a broad landscape of technologies and cancer types.

"These Platform Partnerships are an excellent mix of projects that include advanced technologies as well as technologies in earlier stages of development that have significant potential to exponentially increase progress in all aspects of cancer treatment and diagnosis," said NCI Deputy Director Anna Barker, Ph.D.

And the field of cancer nanotechnology itself becomes strengthened as the teams start working. "Another important feature of the partnerships," Dr. Barker added, "is that they balance a number of well-established researchers with those newly entering the field."

Researchers from Northeastern University, Roger Williams Medical Center, Massachusetts Institute of Technology and Massachusetts General Hospital, for example, have already designed nano-scale carrier molecules to deliver several different drugs to tumor cells all at once, providing not just a one-two punch, but three, four, or five "knockout" steps. Once the cargo has been delivered, the nanocarrier is destroyed, leaving no trace.

"Our next step," said Mansoor Amiji, Ph.D., associate professor of pharmaceutical sciences at Northeastern University and team leader, "is to take this technology to the clinic, with the goal of treating breast and ovarian cancers that have not succumbed via current therapies. The Platform Partnership award is making it possible for our team to optimize and implement this technology to better benefit women with cancer."

Imaging technology is also crucially important in diagnosis and treatment monitoring. Through a unique collaboration between the University of Washington, the Fred Hutchinson Cancer Research Center, Children's Hospital and Regional Medical Center and Philips Medical Systems, children with brain cancer are in the clinical spotlight. This team is developing the nano-scale molecules that will allow oncologists to see the child's cancer at the needle-in-a-haystack stage. These imaging reagents and delivery vehicles are also in preparation to enter the clinic.

"This team has come together to help diagnose and treat medulloblastoma, the most common pediatric brain cancer, and to detect and quantify treatment response as early as possible in our patients," said Raymond Sze, M.D., associate professor of radiology at the University of Washington and team leader. "The NCI has given us the opportunity to develop and test our approaches *in vivo*, enabling us to accelerate clinical translation and direct application to the clinic. Our goal is to significantly enhance diagnosis and treatment while concurrently avoiding the frequently serious side effects associated with current therapies."

In addition to the Platform Partnerships, the NCI's Alliance for Nanotechnology in Cancer encompasses three other programs, including Centers of Cancer Nanotechnology Excellence; multidisciplinary research training and team development awards; and the Nanotechnology Characterization Laboratory. Thus, in just over one year since launch, the Alliance for Nanotechnology in Cancer has put forward one of the largest efforts in the world to apply nanotechnology to biomedical goals.

"Nanotechnology continues to demonstrate a remarkable ability to address the most complex cancer challenges," said Gregory Downing, D.O., Ph.D., director of the Office of Technology and Industrial Relations at NCI. "These four program components are designed to move such promising technologies to the clinic as expeditiously as possible."

A NANO-CANCER GALLERY: The People, Places and Technologies of the NCI Platform Partnerships

Nanotherapeutic Strategy for Multidrug-Resistant Tumors

This Partnership, which includes researchers from Northeastern University, the Roger Williams Medical Center, Massachusetts General Hospital, and Massachusetts Institute of Technology, will develop multifunctional targeted nanoscale devices to deliver therapeutic agents and tumor resistance modulators directly to cancer cells as a means of overcoming multiple-drug resistance. Preliminary work by this team has already produced biodegradable, tumor-targeted drug nanocarriers, and this team is now ready to begin translational efforts to move this research along a development path to the clinic.

Source: Northeastern University

The initial oncology focus of this project will be breast and ovarian cancers. The team, led by Mansoor Amiji, Ph.D., Northeastern University, has expertise in nanoparticle design, pharmaceutical chemistry, cancer biology, and clinical oncology.

DNA-linked Dendrimer Nanoparticle Systems for Cancer Diagnosis and Treatment

This Partnership at the University of Michigan will develop multi-component, dendrimer nanoparticles that will target, image, and treat cancer. The team will first refine technology designed to assemble the various dendrimer components into a multifunctional device, and then begin preclinical testing of the resulting formulations and make extensive use of the NCI's Nanotechnology Characterization Laboratory (NCL) to generate the preclinical safety and pharmacokinetic data needed to move these nanoparticles to the clinic.

The initial focus of this project will be epithelial tumors. The team, led by James Baker, Jr., M.D., University of Michigan, has expertise in dendrimer development, immunology, cancer biology, and clinical oncology.

Metallofullerene Nanoplatform for Imaging and Treating Infiltrative Tumor

This Partnership at the Virginia Commonwealth University will develop metal-based fullerenes (buckyballs), a type of hollow, spherical nanoparticle, to simultaneously deliver imaging agents and anticancer therapeutics to brain tumors known as gliomas.

The initial focus of this project will be brain cancer. The team, led by Panos Fatouros, Ph.D., FACR, Virginia Commonwealth University, has expertise in experimental and clinical imaging, chemistry, neurosurgery, oncology, and tumor targeting. Metal-based fullerenes were invented by one of the Partnership team members.

Detecting Cancer Early with Targeted Nano-Probes for Vascular Signatures

This Partnership, involving researchers from the University of California, San Francisco, and the Burnham Institute, will develop highly specific molecular imaging probes that will enable non-invasive early detection of incipient cancer. These targeted probes will serve as platforms for testing the benefits of new nanotechnology-based imaging agents with improved properties (e.g., higher signal output) forthcoming from the new Centers of Cancer Nanotechnology Excellence and the Cancer Nanotechnology Platform Partnership programs.

Source: University of California, San Francisco

The team, led by Douglas Hanahan, Ph.D., UCSF Comprehensive Cancer Center, UCSF Diabetes Center, has expertise in angiogenesis and mouse models of cancer; vascular profiling; and clinical and experimental molecular imaging.

Photodestruction of Ovarian Cancer: ErbB3 Targeted Aptamer-Nanoparticle Conjugate

This Partnership at the Massachusetts General Hospital is focused on developing multifunctional nanoparticles that can deliver light-activated anticancer compounds specifically to ovarian cancer cells. Once bound to the target cells, the nanoparticles are activated using a miniature endoscopic laser to illuminate only the tumors, providing a second means of ensuring that healthy tissue is spared damage during therapy.

The team, led by Tayyaba Hasan, Ph.D., Massachusetts General Hospital and Harvard Medical School, has expertise in photodynamic therapy, fiber-optic procedures, and nanoparticle design and synthesis.

Hybrid Nanoparticles in Imaging and Therapy of Prostate Cancer

This Partnership at the University of Missouri-Columbia, will use its established expertise in nanomaterial design to create gold nanoparticles capable of imaging molecular abnormalities associated with the earliest stages of prostate cancer. By incorporating gold nanoparticles on cancer specific peptides, the Partnership's investigators hope to create agents that can both image and treat small prostate tumors.

The team, led by Kattesh Katti, Ph.D., University of Missouri-Columbia, has expertise in chemistry, radiology, veterinary sciences, pathology, physics, and biocompatible nanoparticle development.

Near-Infrared Fluorescence Nanoparticles for Targeted Optical Imaging

Source: The University of Texas M. D. Anderson Cancer Center

This Partnership, a collaboration between the researchers at The University of Texas M. D. Anderson Cancer Center and Eastman Kodak, aims to develop novel nanoparticles for targeted molecular optical imaging of early-stage tumors. The fluorescent nanoparticles, developed at Kodak, emit near-infrared fluorescence light that can penetrate deep into tissues. The nanoparticles will be targeted to tumor-associated antigens, reporting their presence or absence in the tumors. Nanoparticles are also designed to respond to enzymatic action which light up only when first activated by enzymes found exclusively on the surface of certain types of cancer cells. The Partnership will focus on studies to fully characterize the biological behavior of these particles and target them to a wide variety of cancer cells.

The initial oncology focus of this project will be brain, breast, and skin cancers. The team, led by Chun Li, Ph.D., The University of Texas M. D. Anderson Cancer Center, has expertise in nanoparticle formulation, imaging science, neurosurgery, and molecular biology.

Integrated System for Cancer Biomarker Detection

This Partnership at the Massachusetts Institute of Technology (MIT) will develop microfluidic devices whose nanochannels are capable of concentrating rare proteins from biospecimens. These devices will then be integrated with another chip-based device to detect and quantify panels of proteins that may serve as early signs of cancer. The devices will be fabricated in such a way as to enable widespread and low-cost distribution for use in the healthcare setting.

The initial oncology focus of this project will be prostate cancer. The team, led by Scott Manalis, Ph.D., Massachusetts Institute of Technology, has expertise in nanofabrication, clinical oncology, and cell biology.

Novel Cancer Nanotechnology Platforms for Photodynamic Therapy and Imaging

This Partnership, which includes team members from the Roswell Park Cancer Institute, the University of Buffalo, and the University of Michigan, will develop targeted nanoparticle platforms for detecting and imaging cancers, and selectively delivering light-activated anti-cancer compounds for guided photodynamic therapy (PDT). Because of the team's extensive experience with the systems they are developing — previous work was funded in part by NCI's Unconventional Innovations Program — this Partnership expects to validate the usefulness of their nanoparticles both for imaging tumors and then killing them with PDT, using models for breast, lung, prostate and colon cancers.

The team, led by Allan Oseroff, M.D., Ph.D., Roswell Park Cancer Institute and University at Buffalo School of Medicine and Biomedical Sciences, has expertise in nanoparticle design, animal models of human cancer, photodynamic therapy, imaging, and clinical oncology.

Multifunctional Nanoparticles in Diagnosis and Therapy of Pancreatic Cancer

Investigators from the State University of New York at Buffalo and Johns Hopkins School of Medicine have combined forces in this Partnership to develop and test multifunctional, hybrid ceramic-polymeric nanoparticles that will deliver imaging and therapeutic agents to pancreatic tumors. This group has a strong history of developing novel, biocompatible nanomaterials — including non-toxic quantum dots — that have the capacity to be targeted to specific types of cancer cells. Based on the prior work by members of this Partnership, they expect to begin translating their work into preclinical and clinical studies in the near-term.

The team, led by Paras Prasad, Ph.D., University at Buffalo, has expertise in materials design and clinical oncology.

Nanotechnology Platform for Targeting Solid Tumors

This Partnership at the Sidney Kimmel Cancer Center will build on extensive experience in nanoparticle development and blood vessel biology to create nanodevices that will target specific cells lining blood vessels in order to improve transit out of the bloodstream and into tumors. Miniaturized probes can be injected into the bloodstream to go throughout the body and not only report back the state of each organ, but actually seek out and treat cancer. This technology has application for imaging and therapy of a wide variety of solid tumors, both primary and metastatic (or disseminated disease) including breast, prostate, kidney, colon and lung.

Source: Sidney Kimmel Cancer Center

The team, led by Jan Schnitzer, M.D., Sidney Kimmel Cancer Center, San Diego, includes chemists, molecular imagers, tumor biologists and molecular biologists.

Nanotechnology Platform for Pediatric Brain Cancer Imaging and Therapy

A collaborative effort among researchers at the University of Washington, the Fred Hutchinson Cancer Research Center, Children's Hospital and Regional Medical Center, and Philips Medical Systems, this Partnership will develop imaging agents and multifunctional nanoscale drug delivery vehicles targeted to medulloblastoma, the most common brain tumor in children. This Partnership will focus on building on its previous research and developing translational efforts to bring this technology into the clinic.

The team, led by Raymond Sze, M.D., University of Washington, has expertise in pediatric brain cancer, tumor molecular biology, magnetic resonance imaging, and materials science.